Express Mail No. EL 500 575 241 US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application of:	Nehls et al.	Confirmation No.:	7547
Serial No.:	09/417,522	Art Unit:	1631
Filed:	October 13, 1999	Examiner:	Moran, M.
For:	Novel Human Polynucleotides and Polypeptides Encoded Thereby	Attorney Docket No:	8535-027

#25
Plunkett
4/1/03
1 of 3

BRIEF ON APPEAL FEE TRANSMITTAL

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

An original and two copies of the applicant's Brief on Appeal in the above-entitled application are submitted herewith. The item(s) checked below apply:

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The brief filing fee is:

☒ Required.
☐ Not required. (Fee paid in prior appeal.)

Please charge the required Brief filing fee to Pennie & Edmonds LLP Deposit Account No. 16-1150. A copy of this sheet is enclosed.

Respectfully submitted,

Date: March 24, 2003

By: JCoruzzi 40,258
Laura A. Coruzzi 30,742
Laura A. Coruzzi (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosure

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Application of: Nehls *et al.*

Serial No.: 09/417,522

Filed: October 13, 1999

For: NOVEL HUMAN POLYNUCLEOTIDES AND POLYPEPTIDES ENCODED THEREBY

Confirmation No.: 7547

Art Unit: 1631

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APPELLANTS' BRIEF ON APPEAL

Laura A. Coruzzi, Esq.
PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

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APPELLANTS' BRIEF ON APPEAL UNDER 37 C.F.R. §§ 1.191 AND 1.192

Pursuant to the provisions of 37 C.F.R. §§ 1.191 and 1.192, an appeal is taken herein from the final rejection of claims 3, and 5-13 of this application. Appellants submit an original and two copies of this appeal brief accompanied by: (1) a Petition for Extension of Time (in duplicate) for three months from December 23, 2002 up to and including March 23, 2003 (which falls on a Sunday), accompanied by the appropriate fee; and (2) a Brief on Appeal Fee Transmittal Sheet (in duplicate). Appellants also submit herewith Exhibit A: an appendix of the claims (*i.e.*, claims 3, and 5-13) under appeal.

I. REAL PARTY IN INTEREST

Appellants have assigned the entire right and interest in the instant application to Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants are not aware of any other appeals or interferences which will directly affect, or be directly affected by, or having a bearing on the Board's decision in the present appeal.

III. STATUS OF CLAIMS

Original claims 1-9 of this application were under prosecution and that the species of SEQ ID NOS:9-18 were elected to facilitate prosecution on the merits. Claims 1, 2, and 4 were canceled without prejudice; claims 3 and 5 were amended; and new claims 10, 11, 12, and 13 were added in an Amendment filed on April 24, 2001. Claims 8, 9, 10, and 13 have been further amended in an Amendment filed on January 17, 2002. Claims 3, and

5-13 have been finally rejected in an Office Action mailed April 23, 2002. A Notice of Appeal was filed on October 23, 2002 appealing the rejection of claims 3, and 5-13.

IV. STATUS OF AMENDMENTS

Subsequent to the final rejection in the Office Action made final dated April 23, 2002, Appellants submitted an amendment under Rule 116 dated October 23, 2002 in an attempt to secure allowance of claims. The amendment has overcome certain rejection but fails to place the application in condition for allowance, as indicated in the Advisory Action from the Examiner mailed November 13, 2002. The Appellants' Brief On Appeal is directed at claims 3, and 5-13. A copy of the claims involved in this Appeal is presented in the attached Exhibit A.

V. SUMMARY OF THE INVENTION

The present invention, as described and claimed, relates to polynucleotides that are disclosed as SEQ ID NOS: 9-18 in the Sequence Listing (claims 3, 10-13). The present invention further relates to an *in vitro* process for producing a polynucleotide that encodes nucleotides of SEQ ID NOS:9, 10, 12-14, and 16-18 (claims 5-9). These polynucleotides are discovered using gene trap technology in human teratocarcinoma cells.

According to the invention, the gene trap vectors used in the invention can integrate into intron sequences of cellular genes ("the trapped genes") in a genome and produce two fusion transcripts. See page 5, lines 12-26; page 75, lines 7-30; and Figures 1A to 1C. The first fusion transcript comprises the coding region of a selectable marker (neomycin resistance was used to produce the presently described polynucleotides) carried within the vector and the upstream exon(s) from the interrupted cellular gene. A mature transcript is generated when the splice donor (SD) and splice acceptor (SA) sites as shown in Figure 1C are spliced together. Translation of this transcript produces a fusion protein that allows for the selection of cells comprising an integrated gene trap vector. The second fusion transcript comprises exon 1 of the murine btk gene within the vector which is fused with exons of the trapped gene that are located downstream of the integration site. Unlike the first fusion transcript, transcription of this transcript is under the control of a vector-borne promoter (such as the PGK promoter), and the corresponding mRNA is generated by splicing between the splice donor (SD) and splice acceptor (SA) sites as shown in Figure 1B. To facilitate isolation of the trapped genes, cDNA was generated by reverse transcribing isolated RNA from pools of human teratocarcinoma cells that have undergone independent gene trap events. Based on the unique sequences present in the first exon of the murine btk gene, selective cloning of the fusion transcript is achieved as shown in Figure 1D and as described on page 76, line 1 to page 77, line 2; page 77, line 23 to page 78, line 29.

Teratocarcinoma cells are the "stem cells" that occur in unusual germ cell tumors and represent a good model for molecular mechanisms of embryonic development and differentiation. These cells generate almost any kind of tissues such as teeth, hair, bone, muscle, and cartilage. Stem cells possess the ability both to produce identical daughter cells (self-renewal), and to produce progeny with more restricted fates (commitment and differentiation). This property of stem cells underpins growth and diversification during development and sustains homeostasis and repair processes throughout adult life. An understanding of molecular mechanisms which govern stem cell fate is therefore of fundamental significance in cell and developmental biology and the capabilities arising from such knowledge have major biomedical applications.

Example 6.1 (pages 74-81; Figures 1A-1D) demonstrated the identification of polynucleotides from human teratocarcinoma cells comprising the claimed nucleic acid sequences of SEQ ID NOS:9-18. It also demonstrated the *in vitro* process for producing a polynucleotide that encodes nucleotides of SEQ ID NOS:9, 10, 12-14, and 16-18 (page 79, line 10 to page 80, line 19).

VI. ISSUES

The following issues are presented for review in this appeal:

A. UTILITY

(1) Whether claims 3, and 5-13 lack patentable utility under 35 U.S.C. § 101 for the lack of a specific, substantial, and credible utility. In the Office Actions dated October 24, 2000, July 17, 2001, April 23, 2002, and an advisory action dated November 13, 2002, the Examiner contended:

(a) that claims 3, and 5-13 are not supported by a specific asserted utility because the disclosed uses of the nucleic acids are not specific and are generally applicable to any nucleic acid;

(b) that the claimed nucleic acids are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter;

(c) since the claimed invention is not supported by a specific and substantial asserted utility, credibility has not been assessed; and

(d) regarding the claimed process of making the nucleic acids, a method of making a compound without utility does not itself have utility.

As discussed below, the Examiner's contentions are in error, and the rejection should be reversed.

(2) Whether claims 3, and 5-13 lack patentable utility under 35 U.S.C. § 112, first paragraph. In the Office Actions dated October 24, 2000, July 17, 2001, April 23, 2002, the Examiner contended that since claims 3, and 5-13 are not supported by either a specific or substantial utility or a well established utility, one skilled in the art would not know how to use the claimed invention.

As discussed below, the Examiner's contention is in error, and the rejection should be reversed.

B. WRITTEN DESCRIPTION

Whether claims 3, and 10-13 contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention under 35 U.S.C. § 112, first paragraph. In the Office Actions dated October 24, 2000, July 17, 2001, April 23, 2002, the Examiner contended that while the specification discloses SEQ ID NOS: 9-18, the specification provides insufficient written description to support the genus of nucleotide sequences that comprise SEQ ID NOS: 9-18 or hybridizes to SEQ ID NOS: 9-18 which are encompassed by claims 3, and 10-13.

As discussed below, the Examiner's contention is in error, and the rejection should be reversed.

VII. GROUPING OF CLAIMS

A. UTILITY UNDER 35 U.S.C. § 101

Claims 3, and 5-13 stand rejected under 35 U.S.C. § 101 for the lack of a specific, substantial, and credible utility. Appellants believe that with regard to the issue of utility under 35 U.S.C. § 101, claims 3, and 5-13 stand or fall together.

B. UTILITY UNDER 35 U.S.C. § 112

Claims 3, and 5-13 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of utility. Appellants believe that with regard to the issue of utility under 35 U.S.C. § 112, first paragraph, claims 3, and 5-13 stand or fall together.

C. WRITTEN DESCRIPTION

Claims 3, and 10-13 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. Appellants believe that with regard to the issue of written description under 35 U.S.C. § 112, first paragraph, claims 3, and 10-13 stand or fall together.

VIII. ARGUMENTS

A. UTILITY OF THE REJECTED CLAIMS

Claims 3, and 10-13 are drawn to polynucleotides that comprise the nucleotide sequences of SEQ ID NOS: 9-18 or that hybridize to polynucleotides that comprise such nucleotide sequences. Claims 5-9 are drawn to *in vitro* processes for producing a polynucleotide of SEQ ID NOS:9-10, 12-14, or 16-18. These claims have been rejected under 35 U.S.C. § 101.

According to 35 U.S.C. § 101, whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter may obtain a patent therefor subject to the conditions and requirements of 35 U.S.C. The threshold of utility is not high. *Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700, 1702 (Fed. Cir. 1999). An invention is "useful" under 35 U.S.C. § 101 if it is capable of providing some identifiable benefit. *Id.* (*citing Brenner v. Manson*, 383 U.S. 519, 534, 148 USPQ 689, 695 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc., 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), emphasis added. Cross v. Iizuka (753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); "Cross"*) states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc., 149 F.3d 1368, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in Diamond vs. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (U.S., 1980)).*

It has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974); In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971).* The specification provides numerous specific, substantial, and credible utilities for the claimed nucleic acids comprising SEQ ID NOS:9-18. For instance, at page 8, lines 12-21, the specification describes the utility of polynucleotides comprising SEQ ID NOS:9-18 for physical and genetic mapping of the human genome and/or the genome of model organisms. Similarly, since the claimed nucleic acids have utility, the process of making these claimed nucleic acids also have utility. As explained in more detail below, the claimed nucleic acids can be used as probes, for example, in Northern blot analysis, or in situ hybridization, for different lineages or different stages of differentiation and development.

1. THE REJECTED CLAIMS HAVE SPECIFIC UTILITY

The Examiner has based the rejection of claims 3, and 5-13 on the contentions that the disclosed uses of the nucleic acids are not specific and are generally applicable to any nucleic acid. The Examiner contended that the specification fails to provide a nexus between specific sequences and a particular gene, disease, splice junction, or chromosome (*See* Office Action dated October 24, 2000, page 5, lines 10-12; and Office Action dated July 17, 2001, page 2, lines 14-16; page 3, lines 9-11).

According to the Examination Guidelines for the Utility Requirement ("Examination Guidelines"), if the applicant has asserted that the claimed invention is useful for any particular practical purpose (*i.e.*, it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the Examiner should not impose a rejection based on lack of utility (66 FR 1098, Jan. 5, 2001).

> "A rejection based on lack of utility should not be maintained if an asserted utility for the claimed invention would be considered specific, substantial, and credible by a person of ordinary skill in the art in view of all evidence of record."

The definition of specific utility may be found in the Revised Interim Utility Guidelines Training Materials. Specific utility is:

> "a utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed." (Http://www/uspto.gov/web/menu/utility).

Unlike the example cited in the above definition where any fragment of genomic DNA can in theory be used as a probe or a chromosome marker, the polynucleotide sequences of SEQ ID NOS: 9-18 have utilities that are not common to any gene in the genome.

Appellants submit that contrary to the Examiner's contention, the polynucleotide sequences of SEQ ID NOS: 9-18 have specific utilities which stem from their cellular origin and the identification process. As explained in the Summary of The Invention hereinabove, gene trap vectors were introduced into human teratocarcinoma cells which led to the identification of gene loci that comprise the sequences set forth in SEQ ID

NOS: 9-18. In particular, as the gene trap vector were introduced into the human teratocarcinoma cell, they integrated into the cell's genome resulting in gene fusions. Each fusion produces a transcript that comprises one or more exons that are located either upstream or downstream from the integration site. These exons, which are portions of a genetic locus that was disrupted by a gene trap vector, are represented by the presently claimed polynucleotides.

Appellants respectfully point out that the genetic loci in the teratocarcinoma cells which have been identified by the gene trap vectors fall within a specific class of genes which are distinct from the broad general class of genes in the genome. Apparently, these identified genetic loci encode genetic functions, the full complement of which are not critically essential to the survival and growth of teratocarcinoma cells. After transfection with the gene trap vectors, the teratocarcinoma cells survived and propagated in culture with only one fully functional allele of the genetic loci. Thus, these genetic loci and the products encoded by these loci are preselected by the transfection and the ensuing cell culture process for possessing functions involved in later stages of cell differentiation and development. Appellants emphasize that the sequences set forth in SEQ ID NOS: 9-18 are not identified from the human genome randomly, rather, they represent a selection of genetic sequences that play a role in the later stages of cellular differentiation and development. Moreover, genes that are critically essential to the survival of teratocarcinoma cells would not have been isolated and propagated by the gene trap methods of the invention, as cells bearing disruptions in such a class of genes would not have been able to survive after transfection with the gene trap vector. Accordingly, the utility of these sequences are not general because not every gene in the genome, when disrupted, necessarily provide the specific utility of the polynucleotides of the invention. Similarly, the processes of making the nucleic acids which have utility, also have utility.

After considering the above arguments presented in the amendment dated January 17, 2002, the Examiner stated in an Office Action dated April 23, 2002 that Appellants do not specifically identify the specific class of genes to which the claimed polypeptides belong. The Examiner further contends that "merely because a disruption in a genetic allele is not lethal is not necessarily evidence that a gene is not involved in 'general survival' or is not a housekeeping gene". Further, the Examiner contends that for the proper function of many genes, one functional copy of the gene is sufficient. In an Advisory Action dated November 13, 2002, the Examiner further contended that the originally filed specification has not established, nor has appellants provided any evidence to support, that genes in cell with higher survival rates are necessarily those which (a) are not involved in house keeping/general survival, or (b) are genes necessarily involved in cellular differentiation and development. The Examiner noted that any gene needed for general survival of a cell is also

a gene required for cellular development, and that genes involved in cellular differentiation may be different and distinct from genes involved in cellular development.

Appellants assert that the identified sequences represent a specific class of genes that is involved in late stages of stem cell differentiation and development. These genetic loci encode genetic functions that are not inhibitors of cell death or apoptosis and are not involved in the general survival, *i.e.*, house-keeping functions, of teratocarcinoma cells because one functional allele of these genes does not trigger cell death or apoptosis and that one functional allele of these genes is sufficient for cell survival and growth. The usefulness of such genes is well-established in the art and are described in the originally filed specification, *inter alia*, at page 12, lines 11-27. Support regarding gene function of the presently claimed polynucleotides can be derived logically as explained below.

The insertion of a gene trapping vector into a gene will interrupt the proper function of that copy of the gene. If the gene is an inhibitor of cell death or apoptosis and both copies are required for normal function, the cell will die and be lost in a population, and the gene will not be identified by the present invention. If the gene is required for cell viability, this reduction of gene activity by 50% will in most cases result in a decrease in cell viability. Thus, in a population of cells exposed to the gene trapping vectors of the invention, the percentage of cells that can be identified as suffering from a 50% reduction in gene activity of a gene required for cell viability is disproportionally lower than the percentage of cells that have a 50% reduction in gene activity of a gene not required for cell viability. On the other hand, in the same population, the percentage of cells with an insertion of the gene trap vector in a gene that is not required for cell viability will be higher than the percentage of cells that have a 50% reduction in gene activity of a gene in the genome that are required for cell viability. As the sequences of the invention are derived from the cells with insertions of the gene trap vector, the number of identified genes that are not required for cell viability will be higher compared to the number of identified genes that are required for cell viability. The gene-trapping method of the present invention therefore pre-selects a class of genes that is not involved in cell viability. Genes that are not involved in cell viability are likely to be involved in late stages of stem cell differentiation and development. Thus, the gene trap method enriches a class of genes that is involved in late stages of stem cell differentiation and development.

As explained above, since the sequences set forth in SEQ ID NOS: 9-18 represent genetic sequences that play a role in late stages of stem cell differentiation and development, the utility of these sequences are not general and are not shared by any random pieces of genomic DNA. Not every gene in the genome necessarily provide this specific utility of the polynucleotides of the invention. Appellants submit that these genetic loci as represented by the presently claimed polynucleotides have substantial utility because they

provide useful information regarding gene expression in teratocarcinoma cells which mimics gene expression during the late stages of stem cell differentiation and development.

Further, the gene trap method identifies genes that would not have been identified by conventional forward genetics. By conventional forward genetics, the cells are mutated and selected for an observable phenotype. Subsequently, the mutation is genetically mapped by following the phenotype. Based on the genetic map position, the gene is cloned. Without an observable phenotype, the mutation cannot be genetically mapped and the associated gene cannot be cloned. The gene trap method, in contrast, pre-selects for a class of genes that is not required for cell viability, and effectively narrows the scope of the identification process. In other words, the present invention allows one to identify genes that do not have an easily observable phenotype. Appellants submit that the claimed polynucleotides are specifically identified and biologically validated (i.e., by actually being spliced) exons that had not been previously identified by conventional molecular biology approaches. These polynucleotides represent transcripts of nominal abundance in conventional cDNA libraries.

Further, the Examiner contends that the claimed invention lacks utility because the specification fails to disclose evidence to support the argument that the sequences of the invention can be used to study development and cell differentiation. The Examiner contends that the claimed invention lacks utility because the Appellants do not specifically identify sequences which are associated with disorders involving development and cell differentiation. Appellants respectfully disagree.

Appellants respectfully point out that the Utility Guidelines provide that, in evaluating evidence related to utility, the character and amount of evidence needed to support an asserted utility will vary depending on what is claimed and whether the asserted utility appears to contravene established scientific principles and beliefs. For the claimed utility to be credible, the invention must be "believable based on the record or the nature of the invention" (M.P.E.P. 2107.02(III)(A). Appellants assert that because of the nature of the invention and for the reasons set forth above, the sequences of the invention which are pre-selected for sequences representing genes that are involved in the differentiation and development of teratocarcinoma cells have credible utility.

The Examiner further contends in an Office Action dated April 23, 2002 that an invention which requires further research in order to have currently available utility fails to meet the utility requirements. In response, Appellants respectfully point out that the pre-selected class of genes have currently available utility in the identification of important regulators of cell differentiation. For example, the sequences identified by the gene trap method can be used to assemble a micro-array. When the micro-array is hybridized with RNA from teratocarcinoma cells of different differentiation stages, genes that are involved

in the differentiation of this type of cells are identified. Using a micro-array with the class of genes that is pre-selected for genes involved in differentiation and development as opposed to cell viability reduces the number of genes that need to be screened compared to a micro-array of genes randomly picked from a genome sequence database. In the Advisory Action dated November 13, 2002, the Examiner contended that the claims are not directed to micro-array and hence argument with respect to micro-array is moot. Appellants submit that micro-array is only an example to demonstrate one of the usefulness of the polynucleotides of the present invention. Hence, although the claims are not directed to such, arguments referring to micro-array are still valid.

Further, the sequences of the invention provide the skilled artisan with probes to isolate the full length cDNA of the genes represented by the sequences of the invention without undue experimentation. The full length cDNAs can be obtained by cDNA library screening with the sequences of the invention. The sequences of those genes are useful for identifying polymorphisms in coding regions and associating those polymorphisms with disorders. For the reasons set forth above, those genes are pre-selected for genes involved in cell differentiation; they can, therefore, be used for developing therapies for disorders involving abnormal cell differentiation.

2. THE REJECTED CLAIMS HAVE SUBSTANTIAL AND CREDIBLE UTILITY

Appellants submit that the specification provides numerous substantial and credible utilities for polynucleotides comprising SEQ ID NOS:9-18.

> Substantial utility is:
>
> > "a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities." (Http://www/uspto.gov/web/menu/utility)

In the context of the utilities that are specific to the claimed polynucleotides, the claimed polynucleotides can be used as probes to facilitate the analysis of genetic loci that play a role during embryonic development and cell differentiation. Appellants submit that the use of probes to investigate stages of embryonic development and cell differentiation constitutes an already identified "real world" context of use. As discussed earlier, since the genetic loci and the products encoded by these loci are preselected for the regulation in later stages of cell differentiation and development, the claimed polynucleotides can be used as probes in hybridization assays well known in the art to determine the activity at the genetic loci during development and differentiation of the teratocarcinomas (*See* for example, page 12, lines 11-27; page 32, line 13 to page 33, line 24).

Teratocarcinomas are totipotent, and as it is well known in the art, that they may differentiate into many different cell types (such as teeth, hair, bone, muscle and cartilage) along various pathways upon induction by certain signals. Each of these pathways may require expression of one or more genes that are disclosed in the specification as filed and represented by the presently claimed polynucleotides. Thus, the claimed polynucleotides can be used as probes, for example, in Northern blot analysis (page 41, line 6), or in situ hybridization (page 41, lines 8-11; page 43, lines 21-29), for undifferentiated teratocarcinomas or differentiated teratocarcinomas of different lineages or at different stages of differentiation and development. The expression pattern of each of these genes can thus be correlated with known or observed events that occur in particular stages of development and cell differentiation. As such, the utility is substantial and credible in a real world context.

The polynucleotides of the invention can also be used for diagnostic gene expression and analysis, for cross species hybridization analysis, antisense inhibition, gene targeting, identifying exon splice junctions, gene therapy, gene delivery and chromosome mapping. *See*, for example, page 12, lines 11-15.

In the Office Actions dated July 17, 2001 and April 23, 2002, the Examiner contended that a "use" to do further research is not considered a specific, substantial, and credible utility. Appellants submit that these genetic loci as represented by the presently claimed nucleic acids have substantial utility not because they can be used to do further research, they have substantial utility because hybridization of a nucleic acid allow inference to useful information; they provide useful information regarding gene expression in teratocarcinoma cells which mimics gene expression during the late stages of stem cell differentiation and development. As such, the claimed polynucleotide as well as the process of making these polynucleotides have substantial utility.

Furthermore, the gene trapped sequences of the present invention overcome some of the limitations of conventional cDNA and expressed sequence tag libraries. In particular, the claimed polynucleotide sequences were identified independent of the level of endogenous mRNA expression of those genes. The gene trap vectors are able to trap even genes that are not expressed or poorly expressed.

Appellants submit that the above described utilities are well known in the art, and hence utilities of the present invention are credible. As stated in the Examination Guidelines for the Utility Requirement, credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure or any other evidence of record (66 FR 1098, Jan 5, 2001). Accordingly, not only do the polynucleotides and the process of making the polynucleotides of the present invention have specific utilities, their utilities are credible and practical.

In view of the foregoing, Appellants submit that the claimed inventions have specific, substantial and credible utility.

B. THE REJECTED CLAIMS HAVE UTILITY UNDER 35 U.S.C.§112, FIRST PARAGRAPH

Claims 3, and 5-13 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking utility.

The Federal Circuit and its predecessor have determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis – the disclosure of a credible utility. *See In re Brana*, 51 F.3d 1560, 1564, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995); *see also In re Jolles*, 628 F.2d 1322, 1326 n. 11, 206 USPQ 885, 889 n. 11 (CCPA 1980); and *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971).

Appellants traverse this rejection on the ground that Claims 3, and 5-13 have significant patentable utility as discussed in Section A, above. Appellants submit that when an Appellant satisfactorily rebuts a rejection based on a lack of utility under 35 U.S.C. § 101, the corresponding rejection imposed under 35 U.S.C. § 112, first paragraph, should also be withdrawn.

C. THE REJECTED CLAIMS AND THE SPECIFICATION MEET THE WRITTEN DESCRIPTION REQUIREMENT

Claims 3, and 10-13 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification. In the Office Action dated July 17, 2001, the Examiner alleges that claims 3 and 10-13 recite open claim language (*i.e.*, comprising) and are therefore also directed to encompass gene sequences, sequences that *hybridize* to SEQ ID NO: 9-18 and that only the specific sequences corresponding to SEQ ID NO: 9-18 meet the written description requirement. The Examiner contends that the species specifically disclosed are not representative of the genus because the genus is highly variant. The rejection is erroneous.

According to applicable case law, an applicant must convey with reasonably clarity to those skilled in the art that the applicant was in possession of the invention. *Vas-Cath v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). "The written description must communicate that which is needed to enable the skilled artisan to make and use the claimed

invention." *Kennecott Corp. v. Kyocera Int'l, Inc.*, 835 F.2d 1419, 1421, 5 USPQ2d 1194, 1197 (Fed. Cir. 1987), *cert. denied*, 486 U.S. 1008 (1988).

Claims 3, 10-13 recite isolated polynucleotides corresponding to one of SEQ ID NOS: 9-18. The isolated polynucleotides are fully described by *structure* or by *physical properties*, or both, sufficient to distinguish the claimed isolated polynucleotides from other materials. Specifically, Applicants assert that the skilled artisan can distinguish the claimed sequences from other sequences and can identify many of the species that the claims encompass. For instance, Claim 3 recites nucleotides that comprise a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS: 9, 12-14, and 16-18. As the exact structure of SEQ ID NOS: 9, 12-14, and 16-18 are provided in the specification, although there are numerous polynucleotides that falls within this description, one person of skilled in the art can readily recognizes the polynucleotide as described in claim 3. Likewise, claim 13 describes a genus of polynucleotides by a property (*i.e.*, hybridizable under defined conditions to known sequences) that readily distinguishes the claimed polynucleotides from other materials. One of skill in the art can readily compare a polynucleotide with the claimed polynucleotides of Claim 13 by performing a hybridization as recited in the claim.

Appellants respectfully point out that the chemical structure of the claimed genus of nucleic acid molecules are described and well known in the art (e.g., DNA, RNA) and that the variation of nucleotide sequence within the claimed genus is also well defined by the functional characteristics of specifically binding under defined hybridizing conditions to nucleic acid molecules of known sequences. According to the Examination Guidelines Under the 35 U.S.C. § 112, ¶ 1, "Written Description" Requirement (66 FR 1099-1111, Jan. 5, 2001), the written description requirement may be satisfied by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See footnote 42 of the Examination Guidelines wherein it is stated that examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length, and also detailed restriction enzyme maps, antibody cross-reactivity, unique cleavage by particular enzymes. One of skill in the art would recognize from the combination of identifying structural and functional characteristics disclosed in the specification that Appellants have possession of the claimed genus of nucleic acid molecules. In fact, the skilled person can readily recognize and determine whether a nucleic acid molecule falls within the pending claims by either comparing the sequence of the molecule with the sequences provided in the application and/or performing a hybridization reaction under

defined conditions with the nucleic acid molecule(s) described in the present application. As such, Appellants submit that adequate written description has been provided.

In the Office Action dated April 23, 2002 and the advisory action dated November 13, 2002, the Examiner contended that the specification lacks written description of the claimed nucleic acids because the claimed sequence may comprise repetitive sequences or entire open reading frames, noncoding regioins, introns, repetitive DNA, regulatory region that are not described in the application.

Appellants submit that the term "comprising" is a term of art that is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. *See Moleculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986), *cert. denied*, 479 U.S. 1030 (1987); *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (Pat. Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). The specification discloses exemplary elements that may be included in the claimed polynucleotides, such as non-coding or regulatory regions (page 23, lines 15-24); vector sequences (page 26, line 19 to page 29, line 12), other coding sequences as obtained by "primer extension" (page 10, line 22 to page 11, line 5). As such, the specification is replete with description of representative elements that may be included in the claimed polynucleotides.

IX. CONCLUSION

For the reasons set forth above, Appellants respectfully request that the rejection of the claims on appeal under 35 U.S.C. §§ 101 and 112 be reversed.

Respectfully submitted,

Laura A. Coruzzi By: [signature] 40,258

Date: March 24, 2003 30,742

Laura A. Coruzzi (Reg. No.)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosures

EXHIBIT A: APPENDIX TO APPELLANTS' BRIEF ON APPEAL

CLAIMS ON APPEAL
Serial No. 09/417,522
Attorney Docket No. 8535-027

3. An isolated polynucleotide comprising a contiguous stretch of at least about 60 nucleotides of at least one of SEQ ID NOS:9, 12-14, 16-18.

5. An *in vitro* process for producing a polynucleotide comprising the steps of:

a) obtaining a polynucleotide template encoding a sequence capable of hybridizing to a gene trapped sequence of SEQ ID NOS:9, 10, 12-14, 16-18;

b) combining said template with a synthetic oligonucleotide sequence of about 14 to about 80 bases in length that comprises a contiguous sequence of at least about 12 nucleotides disclosed in one of SEQ ID NOS:9, 10, 12-14, 16-18; and

c) processing the combined oligonucleotide and template preparation such that said oligonucleotide sequence hybridizes to said template in the presence of a DNA polymerase molecule and a sufficient concentration of dNTPs for said oligonucleotide sequence to prime DNA synthesis by said polymerase,

wherein a polynucleotide is produced that encodes at least about 50 contiguous nucleotides first disclosed in one of SEQ ID NOS:9, 10, 12-14, 16-18.

6. The process of Claim 5 wherein said template is mammalian cDNA.

7. The process of Claim 5 wherein said template is mammalian genomic DNA.

8. The process according to Claim 6 wherein said template is of human origin.

9. The process according to Claim 7 wherein said template is of human origin.

10. An isolated polynucleotide comprising a contiguous stretch of at least about 30 nucleotides of at least one of SEQ ID NO:9, 13, 14, 17, or 18.

11. An isolated polynucleotide comprising a contiguous stretch of at least about 40 nucleotides of at least one of SEQ ID NO:9, 12-14, 16-18.

12. An isolated polynucleotide comprising at least one of SEQ ID NOS:9-18.

13. An isolated polynucleotide of at least about 40 nucleotides capable of hybridizing to a polynucleotide consisting of a sequence selected from the group consisting of SEQ ID NO:9, 12, 13, 14, 16, 17, and 18, under high stringency conditions, said conditions comprising incubating at 65° C in 0.5M $NaHP0_4$, 7% sodium dodecyl sulfate (SDS), 1mM EDTA and washing at 68°C in 0.1xSSC and 0.1% SDS.